

CLAIMS

What is claimed is:

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1. An isolated nucleic acid comprising a nucleotide sequence encoding a polypeptide comprising an LRRCT domain consisting of the amino acid sequence:

N X₁ W X₂ C X₃ C R A R X₄ L W X₅ W X₆ X₇ X₈ X₉ R X₁₀ S S S X₁₁ V

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X₁₂ C X₁₃ X₁₄ P X₁₅ X₁₆ X₁₇ X₁₈ X₁₉ X₂₀ D L X₂₁ X₂₂ L X₂₃ X₂₄ X₂₅ D

X₂₆ X₂₇ X₂₈ C [SEQ ID NO: 19]

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wherein X is any amino acid or a gap and the polypeptide does not comprise the amino acid sequence from residue 260 to 309 of SEQ ID NO: 5 (human NgR1) or SEQ ID NO: 17 (mouse NgR1).

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2. The isolated nucleic acid according to claim 1, wherein X₁₇ and X₂₃ are independently selected from the group consisting of: arginine and lysine.

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3. The isolated nucleic acid according to claim 2, wherein the amino acid sequence of the LRRCT domain is selected from the group consisting of: residues #261-310 of SEQ ID NO: 2 and residues 261-310 of SEQ ID NO: 2 with up to 10 conservative amino acid substitutions.

4. An isolated nucleic acid encoding the polypeptide of SEQ ID NO: 2.

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5. An isolated nucleic acid encoding the polypeptide of SEQ ID NO: 4 (mouse NgR3) or SEQ ID NO: 14 (human NgR3).

6. The isolated nucleic acid according to claim 1, wherein the

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polypeptide comprises: (a) a NTLRRCT domain, and (b) less than a complete CTS domain, provided that a partial CTS domain, if present, consists of no more than the first 39 amino acids of the CTS domain.

5 7. The isolated nucleic acid to claim 1, wherein the polypeptide does not comprise an intact GPI domain.

10 8. An isolated nucleic acid consisting essentially of a nucleotide sequence complementary to a nucleotide sequence encoding a polypeptide selected from the group consisting of: a polypeptide consisting of residues 311-395 of SEQ ID NO: 2, a polypeptide consisting of residues 256-396 of SEQ ID NO: 14 and a polypeptide consisting of residues 321-438 of SEQ ID NO: 4, wherein the nucleic acid is from 8 to 100 nucleotides in length.

15 9. A vector comprising the nucleic acid of any one of claims 1, 4 or 5.

10. A host cell comprising a vector according to claim 9.

20 11. A polypeptide comprising a LRRCT amino acid sequence:
N X₁ W X₂ C X₃ C R A R X₄ L W X₅ W X₆ X₇ X₈ X₉ R X₁₀ S S S X₁₁ V

25 X₁₂ C X₁₃ X₁₄ P X₁₅ X₁₆ X₁₇ X₁₈ X₁₉ X₂₀ D L X₂₁ X₂₂ L X₂₃ X₂₄ X₂₅ D
X₂₆ X₂₇ X₂₈ C [SEQ ID NO: 19]

wherein X is any amino acid residue or a gap and the polypeptide does not comprise the amino acid sequence from residue 260 to 309 of SEQ ID NO: 5 (human NgR1) or SEQ ID NO: 17 (mouse NgR1).

30 12. The polypeptide according to claim 11, wherein X₁₇ and X₂₃ is selected from the group consisting of arginine and lysine.

13. The polypeptide according to claim 11, wherein X_{19} is glycine.

[SEQ ID NO:11]

14. The polypeptide according to claim 11, wherein the amino acid sequence is selected from the group consisting of residues 261-310 of SEQ ID NO:2, 5 residues 206-255 of SEQ ID NO: 14, residues 271-320 of SEQ ID NO:4 and amino acid sequences thereof comprising a conservative substitution.

15. A polypeptide comprising a NTLRRCT amino acid sequence:

10 C P X_1 X_2 C X_3 C Y X_4 X_5 P X_6 X_7 T X_8 S C X_9 X_{10} X_{11} X_{12} X_{13} X_{14} X_{15} X_{16} P
 X_{17} X_{18} X_{19} P X_{20} X_{21} X_{22} X_{23} R X_{24} F L X_{25} X_{26} N X_{27} I X_{28} X_{29} X_{30} X_{31} X_{32} X_{33}
 X_{34} F X_{35} X_{36} X_{37} X_{38} X_{39} X_{40} X_{41} X_{42} L W X_{43} X_{44} S N X_{45} X_{46} X_{47} X_{48} I X_{49}
 X_{50} X_{51} X_{52} F X_{53} X_{54} X_{55} X_{56} X_{57} L E X_{58} L D L X_{59} D N X_{60} X_{61} L X_{62} X_{63} X_{64}
 X_{65} P X_{66} T F X_{67} G L X_{68} X_{69} L X_{70} X_{71} L X_{72} L X_{73} X_{74} C X_{75} L X_{76} X_{77} L X_{78}
 X_{79} X_{80} X_{81} F X_{82} G L X_{83} X_{84} L Q Y L Y L Q X_{85} N X_{86} X_{87} X_{88} X_{89} L X_{90} D
 X_{91} X_{92} F X_{93} D L X_{94} N L X_{95} H L F L H G N X_{96} X_{97} X_{98} X_{99} X_{100} X_{101} X_{102}
 X_{103} X_{104} F R G L X_{105} X_{106} L D R L L H X_{107} N X_{108} X_{109} X_{110} X_{111} V H X_{112}
 X_{113} A F X_{114} X_{115} L X_{116} R L X_{117} X_{118} L X_{119} L F X_{120} N X_{121} L X_{122} X_{123} L
 X_{124} X_{125} X_{126} X_{127} L X_{128} X_{129} L X_{130} X_{131} L X_{132} X_{133} L R L N X_{134} N X_{135} W
 X_{136} C X_{137} C R X_{138} R X_{139} L W X_{140} W X_{141} X_{142} X_{143} X_{144} R X_{145} S S S X_{146}
 V X_{147} C X_{148} X_{149} P X_{150} X_{151} X_{152} X_{153} X_{154} X_{155} D L X_{156} X_{157} L X_{158} X_{159} X_{160}
 D X_{161} X_{162} X_{163} C [SEQ ID NO:18]

25 wherein X is any amino acid residue or a gap and wherein the polypeptide is not the polypeptide of SEQ ID NO: 5 (human NgR1) or SEQ ID NO: 17 (mouse NgR1).

16. The polypeptide according to claim 15, wherein X_6 , X_{37} and X_{38}

30 represents a gap.

17. A polypeptide comprising an amino sequence selected from the

group consisting of: SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:14.

18. The polypeptide according any one of claims 11, 15 or 17, wherein
the polypeptide comprises: (a) an NTLRRCT domain, and (b) less than a complete
5 CTS domain, provided that a partial CTS domain, if present, consists of no more than
the first 39 amino acids of the CTS domain.

19. The polypeptide according to any one of claims 11, 15 or 17,
wherein the polypeptide does not comprise an intact GPI domain.

10 20. The polypeptide according to any one of claims 11, 15 or 17,
wherein the amino acid sequence of the polypeptide further comprises an amino acid
sequence of a heterologous polypeptide.

15 21. The polypeptide according to claim 20, wherein the heterologous
polypeptide is an Fc portion of an antibody.

20 22. A method of producing a polypeptide according to any one of
claims 11, 15 or 17, comprising the steps of introducing an isolated nucleic acid
according to any one of claims 1, 4, 5 or 8 or a vector according to claim 9 into a host
cell, culturing said host cell under conditions suitable for expression of said
polypeptide, and recovering said polypeptide.

25 23. An antibody that binds to a polypeptide of any one of claims 11, 15
or 17.

24. A composition comprising the polypeptide of claim 11, 15 or 17
and a pharmaceutically acceptable carrier.

30 25. A composition comprising the antibody of claim 23 and a
pharmaceutically acceptable carrier.

26. A method of decreasing inhibition of axonal growth of a CNS neuron, comprising the step of contacting the neuron with an effective amount of the polypeptide of claim 11, 15 or 17.

5 27. A method of treating a central nervous system disease, disorder or injury, comprising administering to a mammal an effective amount of the polypeptide of claim 11, 15 or 17.

10 28. A method of decreasing inhibition of axonal growth of a CNS neuron comprising the step of contacting the neuron with an effective amount of the antibody according to claim 23.

15 29. A method of treating a central nervous system disease, disorder or injury, comprising administering to a mammal an effective amount of the antibody according to claim 23.

30. A method for identifying a molecule that binds a polypeptide of claim 11, 15 or 17 comprising the steps of:

20 (a) providing a polypeptide of claim 11, 15 or 17;
(b) contacting the polypeptide with the candidate molecule;
and
(c) detecting binding of the candidate molecule to the polypeptide.

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